12. (Amended) Mouse [~~E~~]embryonic stem cells containing a nucleic acid construct [~~according to claim 1~~] comprising a germline-specific promoter selected from the group consisting of the protamine 1 gene promoter, the protamine 2 gene promoter, the spermatid-specific promoter from the c-kit gene, the sperm-specific promoter from angiotensin-converting enzyme, the oocyte specific promoter from the ZP1 gene, and oocyte specific promoter from the ZP2 gene, operatively associated with a recombinase coding sequence, wherein the nucleic acid construct is in the genome of the stem cells.

13. (Reiterated) Embryonic stem cells according to claim 12 wherein the genome thereof comprises a transcriptionally active selectable marker flanked by two recombinase recombination target sites.

14. (Reiterated) Embryonic stem cells according to claim 13 wherein the recombinase encoded by the recombinase coding sequence operatively associated with a germline-specific promoter is selective for the recombination target sites flanking said selectable marker.

15. (Reiterated) Embryonic stem cells according to claim 13 further comprising one or more of:

a nucleic acid fragment flanked by two recombinase recombination target sites, wherein said recombination target sites are different than the recombination target sites which flank said selectable marker,

a nucleic acid construct comprising an inducible promoter operatively associated with a recombinase coding sequence, or

a nucleic acid construct comprising a tissue-specific promoter operatively associated with a recombinase coding sequence.

18. (Amended) Embryonic stem cells **[~~containing a nucleic acid construct~~]** according to claim **[~~4~~]** 12 wherein said recombinase coding sequence encodes Cre recombinase.

19. (Amended) Embryonic stem cells **[~~containing a nucleic acid construct~~]** according to claim **[~~5~~]** 18 wherein said construct is ProCre, comprising the protamine 1 gene promoter operatively associated with Cre recombinase.

20. (Amended) Embryonic stem cells **[~~containing a nucleic acid construct~~]** according to claim **[~~6~~]** 12 wherein said recombinase coding sequence encodes FLP recombinase.

21. (Amended) Embryonic stem cells **[~~containing a nucleic acid construct~~]** according to claim **[~~7~~]** 20 wherein said construct is ProFLP, comprising the protamine 1 gene promoter operatively associated with FLP recombinase.

22. (Amended) Embryonic stem cells **[~~containing a nucleic acid construct~~]** according to claim **[~~8~~]** 12 wherein said recombinase coding sequence encodes the R gene product of *Zygosaccharomyces*.

23. (Amended) Embryonic stem cells **[~~containing a nucleic acid construct~~]** according to claim **[~~9~~]** 22 wherein said construct is ProR, comprising the protamine 1 gene promoter operatively associated with the R gene product of *Zygosaccharomyces*.

24. (Amended) Embryonic stem cells containing a nucleic acid construct according to claim **[~~10~~]** 23 comprising an inducible promoter operatively associated with a recombinase coding sequence and a transcriptionally active selectable marker flanked by two recombinase recombination target sites in the genome of the stem cells.

26. (Twice Amended) Mouse **[~~E~~]**embryonic stem cells comprising a tissue-specific promoter operatively associated with a recombinase coding sequence and a transcriptionally active selectable marker flanked by two recombinase recombination target sites in the genome of the stem cells.

28. (Twice Amended) A method for excision of the transcriptionally active selectable marker from the embryonic stem cells of claim **[~~13~~]** 26 said method comprising:

passaging the genome derived from said embryonic stem cells through gametogenesis to cause excision of the transcriptionally active selectable marker.

29. (Reiterated) A method according to claim 28 wherein said genome is passaged through spermatogenesis.

30. (Reiterated) A method according to claim 28 wherein said genome is passaged through oogenesis.

31. (Reiterated) A method according to claim 28 wherein said embryonic stem cells further comprise one or more of:

a nucleic acid fragment flanked by two recombinase recombination target sites, wherein said recombination target sites are different than the recombination target sites which flank said selectable marker,

a nucleic acid construct comprising an inducible promoter operatively associated with a recombinase coding sequence, or

a nucleic acid construct comprising a tissue-specific promoter operatively associated with a recombinase coding sequence.

32. (Twice Amended) A method for the production of recombinant alleles in a transgenic animal, said method comprising:

introducing a nucleic acid fragment flanked by at least two recombinase recombination target sites into mouse embryonic stem cells **[~~according to claim 10~~]** comprising a tissue specific promoter operatively associated with a recombinase coding sequence; **[and]**

passaging the genome derived from said embryonic stem cells through gametogenesis to obtain a transformed gamete; and

obtaining progeny from the transformed gamete, thereby producing a transgenic animal having a recombinant allele therein.

34. (Reiterated) A method according to claim 32 wherein said nucleic acid fragment is introduced by homologous recombination, random insertion, retroviral insertion, or site specific-mediated recombination.

35. (Twice Amended) A method for the production of recombinant alleles in a mouse, said method comprising:

introducing a nucleic acid fragment flanked by at least two recombination target sites into mouse embryonic stem cells according to claim [~~13~~] 26,

passaging the genome derived from said mouse embryonic stem cells through gametogenesis without causing recombination of the recombination target sites,

producing offspring resulting from crossing the genome of a gamete produced by the gametogenesis with the genome of a wild type mouse,

whereby the nucleic acid fragment is inserted into the DNA of the offspring so as to produce the recombinant allele therein.

36. (Reiterated) A method according to claim 35 wherein said embryonic stem cells further comprise a second nucleic acid construct selected from the group consisting of a construct comprising an inducible promoter operatively associated with a recombinase coding sequence and a construct comprising a tissue-specific promoter operatively associated with a recombinase coding sequence.

37. (Reiterated) A method according to claim 36 wherein the recombinase encoded by said second construct is expressed in response to inducing conditions.

38. (Reiterated) A method according to claim 36 wherein the recombinase encoded by said second construct is expressed in a tissue selective manner.

39. (Reiterated) A method according to claim 35 wherein the recombination target sites flanking said nucleic acid fragment are recognized by a recombinase which is expressed under the control of an inducible promoter or a tissue specific promoter.

40. (Twice Amended) A method for the production of recombinant alleles, said method comprising:

introducing at least one nucleic acid construct **[~~according to claim 10~~]** comprising an inducible promoter operatively associated with a recombinase coding sequence into mouse embryonic stem cells,

wherein said at least one nucleic acid construct further comprises a nucleic acid fragment flanked by a second pair of recombination target sites and a selectable marker flanked by a first pair of recombination target sites,

passaging the genome derived from embryonic stem cells selected for expression of the marker through gametogenesis to obtain a transformed gamete; and

obtaining first generation progeny **[~~containing the allele~~]** wherein the marker is excised in the germline by crossing the genome of the transformed gamete with the genome of a wild type **[~~animal~~]** mouse.

41. (Reiterated) A method according to claim 40 wherein said first pair of recombination target sites is recognized by a recombinase which is expressed under the control of a germline-specific promoter and said second pair of recombination target sites is recognized by a recombinase which is expressed under the control of an inducible promoter or a tissue specific promoter.

42. (Reiterated) A method according to claim 40 wherein said embryonic stem cells further comprise a second nucleic acid construct selected from the group consisting of a construct comprising an inducible promoter operatively associated with a recombinase coding sequence and a construct comprising a tissue-specific promoter operatively associated with a recombinase coding sequence.

43. (Twice Amended) A method for the conditional assembly of functional gene(s) for expression in eukaryotic cells by recombination of individual inactive gene segments from one or more gene(s) of interest,

wherein each of said segments contains at least one recombinase recombination target site, and wherein at least one of said segments contains at least two recombinase recombination target sites,

said method comprising:

introducing said individual inactive gene segments into **[~~an~~]** a mouse embryonic stem cell according to claim **[~~10~~]** 12 , thereby providing a DNA which encodes a functional gene of interest, the expression product of which is biologically active, upon passage of the genome derived from said embryonic stem cells through gametogenesis.

44. (Twice Amended) A method for the generation of recombinant **[~~livestock~~]** mice, said method comprising:

combining a nucleic acid construct **[~~according to claim 1~~]** comprising a germline-specific promoter operatively associated with a recombinase coding sequence with host pluripotential ES cells derived from early preimplantation embryos, **[~~and~~]**

introducing these embryos into a host female and

allowing the derived embryos to come to term such that a recombinant mouse is thereby produced.